Chapter 16 Outline

- The Respiratory System
- Physical Aspects of Ventilation
- Mechanics of Breathing
- Gas Exchange in the Lungs
- Regulation of Breathing
- Hemoglobin and Oxygen Transport
- CO₂ Transport
- Acid-Base Balance of the Blood

Respiration

- Encompasses 3 related functions: ventilation, gas exchange, and O₂ utilization (cellular respiration)

1. Ventilation moves air in and out of lungs for gas exchange with blood (external respiration)
2. Gas exchange between blood and tissues, and O₂ use by tissues is internal respiration
3. Gas exchange is passive via diffusion

Structure of Respiratory System

- Gas exchange occurs only in respiratory bronchioles and alveoli (= respiratory zone)
- All other structures constitute the conducting zone

Gas exchange occurs across 300 million alveoli
- (60-80 m² total surface area)
- 2 thin cells are between lung air and blood: 1 alveolar and 1 endothelial cell
- Alveolar cells
  - Type 1: Most numerous
  - Type 2: Secrete surfactant

Thoracic Cavity

- Intrapleural space fluid layer between visceral pleura and parietal pleura
- Stick together (potential space) – lungs remain in contact with chest walls

Physical Aspects of Ventilation

- Ventilation results from pressure differences induced by changes in lung volumes
  - Air moves from higher to lower pressure
  - Compliance, elasticity, and surface tension of lungs influence ventilation
Intrapulmonary and Intrapleural Pressures

- Intrapulmonary pressure: pressure within lungs
- Intrapleural pressure: pressure in intrapleural space
- Intrapulmonary – Intrapleural = Transpleural pressure

Fluid keeps lung adhered to chest
Recoil of lung creates inward pull
- = negative intrapleural pressure
During inspiration Intrapulmonary pressure decreases further

During expiration:
- Lungs allowed to recoil and intrapulmonary pressure decreases

Pressure Changes During Quiet Breathing

Positive transpulmonary pressure
- i.e., intrapleural pressure is always less than intrapulmonary!!
- i.e., lungs kept against chest wall
Because intrapleurals is always less than intrapulmonary pressure

Compliance, elasticity, and surface tension of lungs influence ease of ventilation

Compliance
- How easily lung expands with pressure
- Reduced by factors that cause resistance to distension

Elasticity
- Tendency to return to initial size after distension
- elastin proteins!!!
- Tension increases during inspiration - reduced by recoil during expiration
- There is always some elastic tension!

Airway Diameter also influences Airway resistance!

Surface Tension (ST)

- Promotes alveolar collapse - resists distension (expansion)
- Lungs secrete and absorb fluid, normally leaving a thin film of fluid on alveolar surface
  - Film causes ST because H₂O molecules are attracted to other H₂O molecules
  - Thus, ST acts to collapse alveoli;
    - increasing pressure of air within alveoli
- But Phospholipids secreted by Type II alveolar cells lowers ST by getting between H₂O molecules

Mechanics of Breathing:

- Quiet Inspiration
  - diaphragm
  - external intercostals & parasternal intercostals
- Quiet Expiration = passive recoil
- Deep inhalation - add
  - scalenes, pectoralis minor, and sternocleidomastoid
- Deep exhalation
  - internal intercostals, abdominals
Boyle’s Law \((P = \frac{1}{V})\)

### Partial Pressure of Gases

- **Partial pressure** is pressure that a particular gas in a mixture exerts independently
- **Dalton’s Law**: total pressure of a gas mixture is the sum of partial pressures of each gas in mixture
- Atmospheric pressure at sea level is 760 mm Hg
  \[ P_{\text{ATM}} = P_{\text{N}_2} + P_{\text{O}_2} + P_{\text{CO}_2} + P_{\text{H}_2\text{O}} = 760 \text{ mm Hg} \]
- \(H_2O\) vapor decreases pressures of other gases

### Partial Pressure of gases in lungs

- Influence of \(H_2O\) – changes Partial Pressures
- Fully saturated air has a \(P_{\text{O}_2}\) = 47 mmHg
- Low alveolar \(P_{\text{O}_2}\) decreases \(O_2\) uptake
- Low blood flow to alveoli decreases \(O_2\) uptake

### Gas solubility Affects Diffusion

- Movement of gas molecules from air into liquid depend on:
  1. Pressure gradient of the gas
  2. Solubility of the gas in the liquid (how easy it diffuses into liquid)
  3. Temperature (which is largely constant)

\(O_2\) is not very soluble – thus little is dissolved in plasma – it doesn’t have time in alveolar caps to come to equilibrium before blood has left

Compare \(CO_2\) – 20X more soluble than \(O_2\)!

### Gases diffuse down concentration gradients

- normal arterial blood has about \(P_{\text{CO}_2}\) = 100mmHg
- \(P_{\text{O}_2}\) = 40mmHg in systemic veins
- \(P_{\text{CO}_2}\) = 46mmHg in systemic veins

\(CO_2\) solubility is 20 x greater than \(O_2\); i.e., despite much lower partial pressure of \(CO_2\) equal amounts of 2 gases are exchanged
Pulmonary Circulation

- Rate of blood flow through pulmonary circuit equals flow through systemic circulation
- Pumped at lower pressure (about 15 mm Hg)
- Pulmonary vascular resistance is low!
- Low pressure produces less net filtration than in systemic capillaries
- Pulmonary arterioles constrict where alveolar $P_{O_2}$ is low and dilate where its high!!
- This matches ventilation to perfusion (blood flow)

Regulation of Breathing: Brain Stem Respiratory Centers

- Automatic breathing is generated by a rhythmicity center in medulla oblongata
- Dorsal/Ventral Respiratory groups
- Inspiratory neurons stimulate nerves that innervate respiratory muscles
-Expiration occurs when expiratory neurons inhibit phrenic nerve
- Pacemaker cells

CNS Control of Breathing

Effects of Blood $P_{CO_2}$ and pH on Ventilation

- Chemoreceptors modify ventilation to maintain homeostasis of $CO_2$, $O_2$, and pH levels
  - $P_{CO_2}$ is most crucial because of its effects on blood pH
    - $H_2O + CO_2 <--> H_2CO_3 <--> H^+ + HCO_3^-$
    - Carbonic Acid
    - Bicarbonate
  - Also, $P_{CO_2}$ (and $H^+$) more influenced by breathing changes compared to $O_2$ because lots of “stored” $O_2$
**Effects of Blood $P_{CO_2}$ and pH on Ventilation**

- Medulla oblongata chemoreceptors (central chemoreceptors) have effect on ventilation
  - Monitor $CO_2$ – kind of!
    - $H^+$ can't cross BBB but $CO_2$ can
  - Low $pH$ causes increase in breathing
  - Rate and depth of ventilation adjusted to maintain arterial $P_{CO_2}$ of ~40 mm Hg
- **Peripheral chemoreceptors**: respond to $PO_2$, $P_{CO_2}$, $pH$ - aorta & carotid arteries
  - Increase in $PCO_2$ or decrease in $O_2$ or $pH$ causes increased ventilation

**Pulmonary Receptors & Ventilation**

- Lungs have receptors that influence brain respiratory control centers via sensory fibers in vagus nerve
  - Unmyelinated C fibers stimulated by noxious substances such as capsaicin
    - Causes apnea followed by rapid, shallow breathing
  - **Irritant receptors** are rapidly adapting; respond to smoke, smog, and particulates
    - Causes cough
  - **Stretch receptors** activated during inspiration (Hering-Breuer reflex)
    - Inhibits respiratory centers to prevent over-inflation of lungs

**Hemoglobin (Hb) and $O_2$ Transport**

- Loading of Hb with $O_2$ occurs in lungs; unloading in tissues
- Affinity of Hb for $O_2$ changes with a number of physiological variables
- Each RBC has about 280 million molecules of Hb
- Most $O_2$ in blood is bound to Hb inside RBCs as oxyhemoglobin
  - It's a week bond between $O_2$ and hemoglobin
  1. Depends on the $PO_2$ in plasma surrounding the red blood cells
  2. Number of potential Hb binding sites available in red blood cells

- **In anemia**, Hb levels are below normal
- **In polycythemia**, Hb levels are above normal

  Hb production controlled by **erythropoietin (EPO)**
  - Production stimulated by low $Po_2$ in kidneys

- High $P_{O_2}$ of lungs favors loading; low $P_{O_2}$ in tissues favors unloading
**Oxhemoglobin**

- Systemic arteries with \( P_{O_2} \) of 100 mmHg have a percent oxhemoglobin of 97%
  - i.e., 97% of the hemaglobin is bonded to oxygen
  - i.e., 97% is in the form of oxyhemaglobin
- Blood leaving tissue capillaries is \( P_{O_2} \) of 40 mmHg and has a percent oxhemoglobin of ~75%.

**Key factor that drives bonding (and unbinding) is** \( P_{O_2} \)

- Hemoglobin + \( O_2 \) \( \rightarrow \) Oxyhemoglobin
  - High \( P_{O_2} \) = bonding \( O_2 \) to hemaglobin
  - Low \( P_{O_2} \) = dissociation of oxyhemaglobin

**Oxyhemoglobin Dissociation Curve**

- Provides % of Hb that have bound \( O_2 \) at different \( P_{O_2} \)
- Reflects loading and unloading of \( O_2 \)
- Where \( P_{O_2} \) is high OxyHb occurs
- Where \( P_{O_2} \) is low OxyHb dissociates

- In steep part of curve, small changes in \( P_{O_2} \) cause big changes in % saturation of hemoglobin

**\( P_{O_2} \) (mm hg)**

Shifting curve to right = lowers affinity of oxyhemoglobin bond - more likely to unload \( O_2 \)

**Another factor: Effect of 2,3 DPG on \( O_2 \) Transport**

- RBCs have no mitochondria; can't perform aerobic respiration
  - 2,3-DPG (2-3 disphosphoglyceric acid) is a byproduct of glycolysis in anaerobic respiration in RBCs
  - 2,3 DPG lowers affinity of Hb for \( O_2 \)
    - i.e. high levels of 2,3 DPG increases unloading of \( O_2 \)
- Enzyme that produces 2,3-DPG is inhibited by Oxyhemaglobin
  - i.e., Saturated Hb inhibits 2,3-DPG formation
  - i.e., 2,3-DPG formation production increased by low oxyhemaglobin
- High altitude & anemia increase 2,3 DPG production – lowers Hg affinity for \( O_2 \)

**Myoglobin**

- Has only 1 globin; binds only 1 \( O_2 \)
- Has higher affinity for \( O_2 \) than Hb; is shifted to extreme left
- Releases \( O_2 \) only at low \( P_{O_2} \)
- Serves as \( O_2 \) storage, in heart (systole) & skeletal muscles

**CO2 Transport**

- \( CO_2 \) transported in blood
  1. **dissolved \( CO_2 \)** (10%)
  2. **carbaminohemoglobin** (20%)
  3. **bicarbonate ion**, \( HCO_3^- \), (70%)

- In RBCs **carbonic anhydrase** catalyzes formation of \( H_2CO_3 \) (carbonic acid) from \( CO_2 + H_2O \)

  \[ H_2O + CO_2 \leftrightarrow H_2CO_3 \]
CO2 transport in Blood

- Blood pH is maintained within narrow pH range by lungs and kidneys (normal = 7.4)
- Most important buffer in blood is bicarbonate
  - \( \text{H}_2\text{O} + \text{CO}_2 \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- \)
  - Excess H+ is buffered by HCO_3-
  - Kidney’s role is to excrete H+ into urine

Reverse Chloride Shift

- In lungs, \( \text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- \), moves to left as \( \text{CO}_2 \) is breathed out
- Binding of \( \text{O}_2 \) to Hb decreases its affinity for H+
  - H+ combines with HCO_3- and more \( \text{CO}_2 \) is formed
- Cl- diffuses down concentration and charge gradient out of RBC (reverse chloride shift)

Acid-Base Balance of the Blood

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Bicarbonate as a buffer
Acid-Base Balance of the Blood

- **Acidosis** is when pH < 7.35; **alkalosis** is pH > 7.45
- **Respiratory acidosis** caused by hypoventilation
  - Causes rise in blood CO$_2$ and thus carbonic acid
  - Hypoventilation causes high CO$_2$ (hypercapnia)
- **Respiratory alkalosis** caused by hyperventilation
  - Results in too little CO$_2$
  - Hyperventilation causes low CO$_2$ (hypocapnia)

Ventilation and Acid-Base Balance

- Ventilation usually adjusted to metabolic rate to maintain normal CO$_2$ levels
- Hypoventilation: not enough CO$_2$ is removed from lungs
  - Acidity builds, causing respiratory acidosis
- Hyperventilation: too much CO$_2$ is removed
  - pH rises, causing respiratory alkalosis
- Dizziness: decrease in CO$_2$ causes pH of CSF to increase = alkadosis results in cerebral vasoconstriction